REMARKS

In the Claims

Dependent claims 11, 12, 14, 17 and 18 are amended to be dependent on independent claim 19. The method claims are amended to use language corresponding to the language of the device claims.

Election/Restrictions

Applicants acknowledge the withdrawal of claims 20-26 from consideration. Applicant requests that, upon allowance of the product claims, the withdrawn process claims be rejoined.

The Rejections under Section 103

Claims 10-12 and 19 were rejected as allegedly unpatentable over JP 3-255037 in view of Takada (5,637,319). A translation of JP 3-255037 is attached.

JP 3-255037 teaches a glycyrrhizin preparation coated with an enteric film; however, JP 3-255037 fails to teach or suggest the device for colon-targeted oral delivery of claim 19, and its dependent claims or of claim 10. Nowhere does the reference, for example, teach or suggest a shaped core made of a glyceride suppository base that melts or liquefies at the body temperature. Instead, the reference teaches a liquid dispersion in a coated capsule (Example 1), coated granules (Example 2), and a liquid dispersion in soft capsules (Example 3).

Examples 1 and 3 are directed to dispersions dissolved in "Invider 742," identified as a mixture of mixture of mono-, di- and tri-glycerides of capric (C_{10}) acid and caprylic (C_8) acid. Both of these dispersions, are believed to be liquid at room temperature. Example 3 specifically states that the dispersion is liquid, and Example 1, states that the dispersion was filled into a capsule. The fact that these dispersions were liquid at room temperature is also supported by the absorption test discussed on page 7 of the reference, wherein a dispersion of glycyrrhizin monoammonium salt in Invider 472 was administered to the duodenum of rats. Upon belief, a dispersion other than liquid can not be directly administered to the duodenum of rats.

Example 2 is directed to granules formed from pulverized glycyrrhizin and stearic (C_{16}) acid monoglyceride. The number of carbon atoms are larger for stearic (C_{16}) acid

monoglyceride than for capric (C_{10}) acid and caprylic (C_8) acid. Thus, the components are solid in form and the resultant dispersion is in the form of granules, and not a liquid. Thus, neither these examples, nor as the rest of the specification, teach or suggest a shaped core made of a glyceride suppository base that melts or liquefies at the body temperature.

Takada also does not offer any teaching or suggestion for the preparation of such a shaped core.

Additionally, JP 3-255037 teaches that the enteric film is dissolved in the duodenum whereby glycyrrhizin is rapidly absorbed in the duodenum and the small intestine. See page 3, lines 4-9. The Examiner's reliance on the alleged broad definition of "enteric" from Webster's dictionary, i.e., "medical preparation treated to pass through the stomach unaltered and disintegrated in the intestines," is misplaced since JP 3-255037 specifically teaches that the enteric film is dissolved in the duodenum. Nowhere does this reference teach or suggest that the film enclosing the liquefied core ruptures selectively in the colon by the internal pressure generated by the peristalsis of the intestine. Broadening the teaching of the reference based on a dictionary definition of a term therein is impermissible when the reference itself clearly defines the scope of such a term. One of ordinary skill in the art would have construed the definition of enteric in accord with the teachings of the reference and not in accord with a broader dictionary definition.

On the other hand, Takada teaches an ethylcellulose capsule which is disintegrated by the inner pressure of the large intestine. See column 3, lines 1-14. One of skill in the art would not have been motivated to select this capsule for the dispersions of JP 3-255037 since the latter are directed to increasing the concentration of glycyrrhizin in the blood when released in the duodenum. Thus, the coating taught by Takada would not have achieved the objectives of JP 3-255037, i.e., to deliver the dispersions to the duodenum.

Furthermore, although not necessary for the patentability of the invention, none of the cited references teach a film coating that is formed by dipping the shaped core in a solution of ethylcellulose or a film that is continuous around a shaped core. JP 3-255037 teaches enteric films which dissolve in the duodenum. Some specific compounds for the formation of the films are named on page 3, lines 13-16. Ethylcellulose is not among them. Takada teaches a variety of capsules, one of which is an ethylcellulose capsule. However, that capsule is formed by coating the inner or outer surface of a conventional gelatin capsule body and then

dissolving the gelatin in warm water. See column 7, lines 59-64, and column 8, lines 15 to 18.

Further, Takada teaches that a pore is made in the capsule to fill the drug into the capsule followed by closing the pore with ethylcellulose glue or by capping the opening with an ethylcellulose cap. See column 8, lines 18-35, and Examples 4 to 6. Therefore, the final product of Takada has a capsule that either has a cap or a pore that is sealed by glue instead of a capsule of the present invention which is continuous (see claim 19). Thus, the coating of the present invention differs from coatings described in each of the prior art references. No teaching of suggestion to alter the prior art coatings is present in any of the references. Thus, the advantages, i.e., simple inexpensive procedure, achieved by the preparation of a coating in accord with the present invention is not taught or suggested by either of the references.

Also, forming a coating in accord with the present invention would not be possible over the liquid dispersions of the primary reference. One would not be able to dip the liquid dispersion in a solution of ethylcellulose to form a film that is continuous around said liquid dispersion, as can be done with a shaped core. As for the granules, the reference only teaches and suggests their coating with a coating that dissolves in the duodenum, i.e., one of the mentioned coatings on page 3 that is taught to dissolve in the duodenum.

The Office Action alleges that "the intended use of the enteric coating whether is dissolved or ruptured, does not hold patentable weight unless a structural difference in the end product is shown." The test for obviousness is whether the combined teachings of the references would have suggested the claimed invention to those of ordinary skill in the art. The current invention is directed to a device for colon-targeted oral delivery which has several features that are not taught or suggested in the prior art references. These features make the claimed oral delivery device structurally different than the prior art devices in at least having a shaped core that melts or liquefies at body temperature, and/or a continuous (see claim 19) coating film of ethylcellulose enclosing said shaped core.

Additionally, even if one were to view the broad dictionary definition as controlling in the JP 3-255037 reference, which is not the case, a reference must be evaluated not for only what it teaches broadly, but also for what it fairly suggests to a skilled artisan, i.e., what it specifically motivates the artisan to do to practice the taught art. While a broad teaching or goal of an invention may motivate an artisan to try a variety of solutions to a recognized problem, i.e., make it obvious to try, it does not render all solutions to said problem obvious.

The standard in patent law is not obvious to try. "A general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out." *In re Deuel*, 51 F.3d 1552, 34 USPQ2d 1210 (Fed. Cir. 1995). Thus, a general incentive to provide an enteric coating on a given composition does not provide the motivation to use any known enteric coating. Obviousness is tested by "what the combined teachings of the references would have suggested to those of ordinary skill in the art." *In re Keller*, 642 F.2d 413, 425, 208 USPQ 871 (CCPA 1981).

Thereafter, even if JP 3-255037 is construed to teach an enteric coating broadly, i.e., in accord with the alleged dictionary definition, that teaching is insufficient to render obvious any specific enteric coating without further evaluating what the reference specifically suggests. JP 3-255037, as discussed above, teaches the delivery of glycyrrhizin to the duodenum, while the secondary reference teaches a capsule that ruptures in the large intestine. No motivation is thus present to use the capsule of the secondary reference for the delivery of the drugs of the primary reference. The claims are thus not obvious.

Claims 13 and 15 were rejected as allegedly unpatentable over JP 3-255037 in view of Takada (5,637,319) in further view of Sipos (4,079,125). Claims 14 and 16 were rejected as allegedly unpatentable over JP 3-255037 in view of Takada (5,637,319) in further view of JP 10226650. Finally, claims 17 and 18 were rejected as allegedly unpatentable over JP 3-255037 in view of Takada (5,637,319) in further view of Antoku (5,434,142).

These claims are all dependent claims, and are allowable for the reasons discussed above.

Accordingly, applicants at this point do not burden the record with arguments to the allegations.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned **"Version With Markings To Show Changes Made"**.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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Version With Markings To Show Changes Made

In the Claims

The claims have been amended as follows:

11. (Twice Amended) The device according to claim ~~10~~ 19, wherein said amount of glycyrrhizin is in excess of the amount needed for compensating for the hydrolysis thereof by the intestinal flora.

12. (Twice Amended) The device according to claim ~~10~~ 19, wherein said coating film is formed by dipping the shaped core in a solution of ethylcellulose.

14. (Twice Amended) The device according to claim ~~10~~ 19, wherein said shaped core further contains an absorption promoter for glycyrrhizin.

17. (Amended) The device according to claim ~~10~~ 19, wherein the device contains 10 to 1,000 mg of glycyrrhizin.

18. (Amended) The device according to claim ~~10~~ 19, wherein the device contains 100 to 800 mg of glycyrrhizin.

20. (Amended) A process for preparing a colon-targeted oral delivery ~~system~~ device of glycyrrhizin comprising:

(a) adding glycyrrhizin to a glyceride suppository base that melts or liquefies at the body temperature while the suppository base is in molten or liquefied state to obtain a suspension;

(b) casting the suspension in a mold;

(c) cooling the mold to obtain a shaped solidified core of the suspension;

(d) enclosing the resultant shaped core with a continuous coating film of ethylcellulose, the coating film having a film thickness whereby when the ~~system~~ device is transported through the digestive tract to the colon, the film enclosing the liquefied core

ruptures selectively in the colon by the internal pressure generated by the peristalsis of the intestine.

26. (Amended) The colon-targeted oral delivery ~~system~~ device prepared by the process of claim 20.